STN- Structure Search
5-17-05

10/684,212

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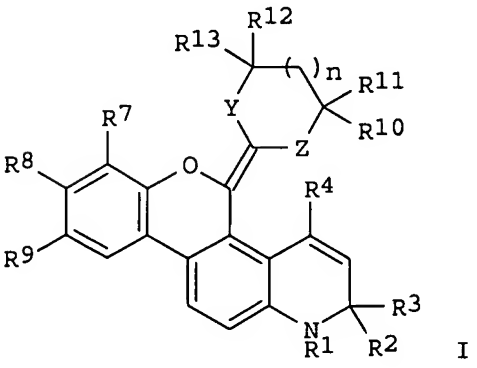
L7 ANSWER 1 OF 2 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:333720 CAPLUS
DOCUMENT NUMBER: 140:339316
TITLE: Preparation of 5-(cycloalkyl)methylidene-1,2-dihydro-5H-chromeno[3,4-f]quinolines as selective progesterone receptor modulators.
INVENTOR(S): Zhi, Lin; Van Oeveren, Cornelis Arjan
PATENT ASSIGNEE(S): Ligand Pharmaceuticals Incorporated, USA
SOURCE: PCT Int. Appl., 41 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004033459	A1	20040422	WO 2003-US24416	20030804
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2004147530	A1	20040729	US 2003-684227	20031010

PRIORITY APPLN. INFO.: US 2002-418140P P 20021011
OTHER SOURCE(S): MARPAT 140:339316
GI



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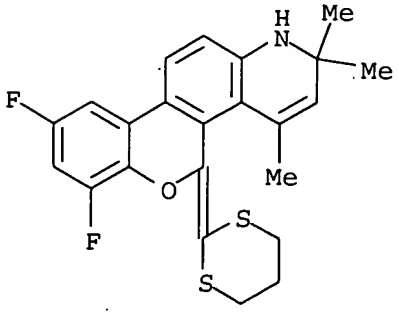
AB Title compds. [I; R1 = H, alkyl, haloalkyl, heteroalkyl, COR5, C02R5, S02R5, CONR5R6; R2, R3 = H, alkyl, haloalkyl; R2R3 = atoms to form a cycloalkyl ring; R4 = H, F, Cl, Br, CN, OR5, alkyl, haloalkyl, heteroalkyl; R5, R6 = alkyl, heteroalkyl, haloalkyl; R7-R9 = H, F, Cl, Br, iodo, NO2, CN, OR5, NR5R6, SR5, COR5, C02R5, CONR5R6, alkyl, heteroalkyl, haloalkyl, alkenyl, alkynyl; R10-R15 = H, F, Cl, Br, OR5, alkyl, haloalkyl, heteroalkyl; R12R14 = bond when Y = CR14R15; R10R14 = bond when Z = CR14R15; Y, Z = O, S, NR6, CR14R15; n = 0-3], were prepared Thus, to 1,3-dithiane in THF at -70° was added BuLi in hexane and the resulting mixture was stirred at -10° for 2 h. To the reaction mixture

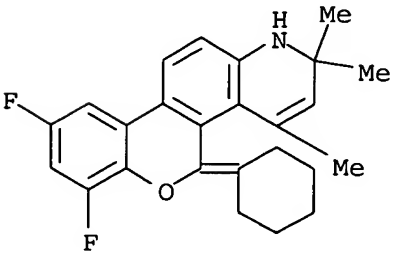
at -70° was added 9-fluoro-1,2-dihydro-2,2,4-trimethyl-5-chromeno[3,4-f]quinoline in THF; the dark red solution was slowly warmed to -30 till the red color faded away and was quenched with H2O to give 9-fluoro-5-(1,3-dithia-2-cyclohexyl)-5-hydroxy-1,2-dihydro-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline. The latter was stirred in CH2Cl2 with catalytic TsOH for 15 h to give 42% 9-fluoro-5-(1,3-dithia-2-cyclohexylidene)-1,2-dihydro-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline. This showed progesterone receptor agonist activity with IC50 = 2.0 nM.

IT **681146-25-8P 681146-28-1P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(claimed compound; preparation of cycloalkylmethylidenechromenoquinolines as selective progesterone receptor modulators)

RN 681146-25-8 CAPLUS
CN 1H-[1]Benzopyrano[3,4-f]quinoline, 5-(1,3-dithian-2-ylidene)-7,9-difluoro-2,5-dihydro-2,2,4-trimethyl- (9CI) (CA INDEX NAME)

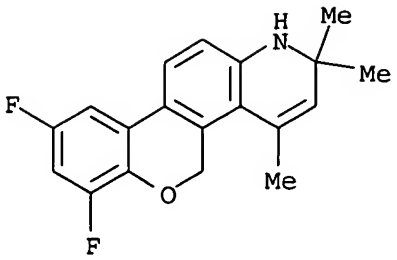


RN 681146-28-1 CAPLUS
CN 1H-[1]Benzopyrano[3,4-f]quinoline, 5-cyclohexylidene-7,9-difluoro-2,5-dihydro-2,2,4-trimethyl- (9CI) (CA INDEX NAME)



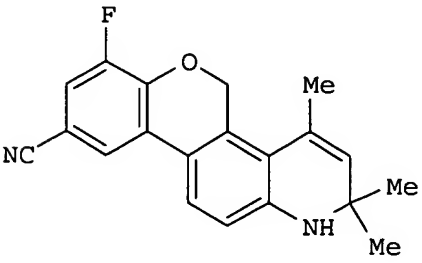
IT **602296-45-7**
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of cycloalkylmethylidenechromenoquinolines as selective progesterone receptor modulators)

RN 602296-45-7 CAPLUS
CN 1H-[1]Benzopyrano[3,4-f]quinoline, 7,9-difluoro-2,5-dihydro-2,2,4-trimethyl- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 2 OF 2 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:405952 CAPLUS
DOCUMENT NUMBER: 139:261186
TITLE: Development of progesterone receptor antagonists from 1,2-dihydrochromeno[3,4-f]quinoline agonist pharmacophore
AUTHOR(S): Zhi, Lin; Ringgenberg, Josef D.; Edwards, James P.; Tegley, Christopher M.; West, Sarah J.; Pio, Barbara; Motamedi, Mehrnouch; Jones, Todd K.; Marschke, Keith B.; Mais, Dale E.; Schrader, William T.
CORPORATE SOURCE: Discovery Research, Ligand Pharmaceuticals, San Diego, CA, 92121, USA
SOURCE: Bioorganic & Medicinal Chemistry Letters (2003), 13(12), 2075-2078
CODEN: BMCLE8; ISSN: 0960-894X
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 139:261186
GI



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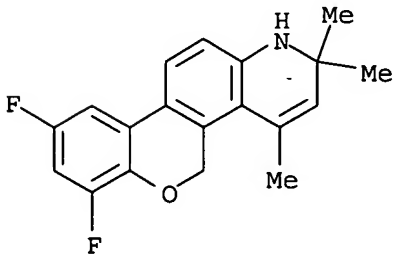
AB A series of 1,2-dihydrochromeno[3,4-f]quinoline derivs., e.g. I, was synthesized and tested in biol. assays to evaluate the nonsteroidal progesterone receptor (hPR) modulator pharmacophore as antiprogestins. A number of potent analogs were identified by modification of the substituents at the D-ring. The cross-reactivity of selected new nonsteroidal hPR antagonists with other steroid receptors was assessed using human androgen (hAR), glucocorticoid (hGR), estrogen (hER), and mineralocorticoid receptor (hMR) co-transfection assays. No agonist activity was observed for any of the test compds., but antagonist activities were detected, most notably on hAR and hGR. However, several new compds. still offered an improved cross-reactivity profile in comparison with Mifepristone. The separation of hPR antagonist activity over hAR and hGR was generally greater for the more active analogs. In summary, the new nonsteroidal series

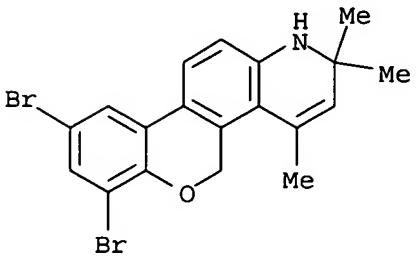
exhibited potent hPR antagonist activity with improved cross-reactivity profile. The SAR study, in addition to our early results in the area, provide new opportunities to develop both receptor- and tissue-selective hPR antagonists.

IT **602296-45-7P 602296-48-0P 602296-49-1P 602296-50-4P**
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent)
(preparation and structure activity of progesterone receptor antagonists from dihydrochromenoquinoline agonist pharmacophore)

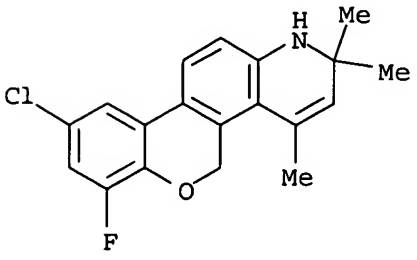
RN 602296-45-7 CAPLUS
CN 1H-[1]Benzopyrano[3,4-f]quinoline, 7,9-difluoro-2,5-dihydro-2,2,4-trimethyl- (9CI) (CA INDEX NAME)



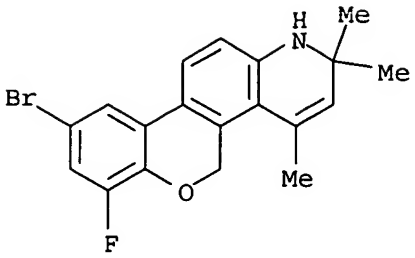
RN 602296-48-0 CAPLUS
CN 1H-[1]Benzopyrano[3,4-f]quinoline, 7,9-dibromo-2,5-dihydro-2,2,4-trimethyl- (9CI) (CA INDEX NAME)



RN 602296-49-1 CAPLUS
CN 1H-[1]Benzopyrano[3,4-f]quinoline, 9-chloro-7-fluoro-2,5-dihydro-2,2,4-trimethyl- (9CI) (CA INDEX NAME)



RN 602296-50-4 CAPLUS
CN 1H-[1]Benzopyrano[3,4-f]quinoline, 9-bromo-7-fluoro-2,5-dihydro-2,2,4-trimethyl- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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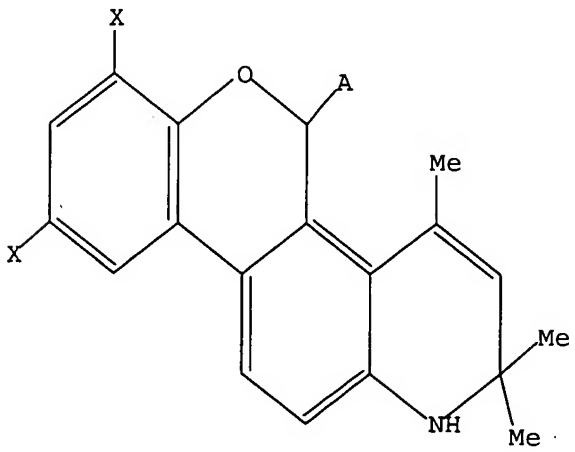
(FILE 'HOME' ENTERED AT 11:36:44 ON 17 MAY 2005)

FILE 'REGISTRY' ENTERED AT 11:36:54 ON 17 MAY 2005
L1 STRUCTURE UPLOADED
L2 0 S L1
L3 0 S L1 FULL
L4 STRUCTURE UPLOADED
L5 0 S L4
L6 6 S L4 FULL

FILE 'CAPLUS' ENTERED AT 11:40:16 ON 17 MAY 2005
L7 2 S L6

=> d l1
L1 HAS NO ANSWERS
L1 STR



Structure attributes must be viewed using STN Express query preparation.

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